EAGAR Importance Rating and Summary of Antibiotic Uses in Humans in Australia

Background

The Expert Advisory Group on Antimicrobial Resistance of the NH&MRC provides advice to Australian governments and their agencies on risk minimisation strategies for controlling antibiotic resistance in Australia. As part of this activity, EAGAR undertakes/oversees risk assessments for new antibiotics and extensions of indications of currently registered antibiotics. The importance of the antibiotic or class of antibiotics in human medicine is taken into account in these risk assessments.

Purpose

This table is intended to provide guidance to clinicians and the pharmaceutical industry (human and animal) about the importance of the various antibacterial agents available for human use in Australia. If an antibiotic is classified as "High", it implies that if resistance develops there will be very limited or in some cases no alternatives available to treat serious bacterial infections. It is based on a table published originally in the JETACAR report (Joint Expert Technical Advisory Committee on Antibiotic Resistance).

Details are also given on the current ways in which all antibiotics are used in humans. This list is for guidance only, and does not include every use of the agent or class. All agents with significant antibacterial activity are included in the table, even if their primary use is for other than treatment of bacterial infections (e.g. pyrimethamine, a dihydrofolate reductase inhibitor whose main role is treatment of malaria and toxoplasmosis, but with the same antibacterial activity as trimethoprim).

EAGAR uses this information as a guide in providing advice to regulatory agencies and government committees including the NRA, TGA, NDPSC and the PBAC, as a method of assessing the risk to human health after exposure of susceptible humans to either an antibiotic or antibiotic-resistant bacteria. In risk assessment terms, this table is relevant to the "severity of impact' which is an important element to overall risk characterisation. As an example, if an antibiotic is rated as 'High', EAGAR would consider that the severity of impact caused by bacteria resistant to that antibiotic is high, as there are few or no alternatives to many infections. Rating in this table does not affect other parts of risk assessment including hazard, exposure, impact or probability of disease as a result of exposure.

EAGAR ratings will change over time as resistance levels change, new drugs are introduced, and optimum drug choices alter because of new medical evidence. Consequently the table will be updated at regular intervals

Antibiotic	EAGAR Rating	Uses P, T, R	Comments on Use in Human Medicine
Narrow-spectrum penicillins			
Benzylpenicillin (pen G) and phenoxymethylpenicillin (pen V)	Low	P2, T3, R1	Primary agents in pneumococcal and streptococcal infection
Procaine penicillin	Low	P2, T3, R1	Intramuscular – occasional substitute for benzylpenicillin
Benzathine penicillin	Low	P3, T3, R1	Intramuscular – syphilis treatment and rheumatic fever prophylaxis
Moderate-spectrum penicillins			
Amoxycillin and ampicillin	Low	P2, T3, R1	Principal role in respiratory tract infections; widespread IV hospital use in combination for a range of moderate and serious infections. Surgical and endocarditis prophylaxis
Antipseudomonal penicillins			
Piperacillin	High	P1, T3, R3	Primary agent for *Pseudomonas aeruginosa*
Antistaphylococcal penicillins			
Cloxacillin, dicloxacillin and flucloxacillin (methicillin)	Medium	P3, T3, R1	Standard treatment for *Staphylococcus aureus* infections (not MRSA). Surgical prophylaxis, especially orthopaedics
ß-lactamase inhibitor combinations			
Amoxycillin-clavulanate	Medium	P1, T3, R1	Second line agent for respiratory tract infections; role in certain types of skin/soft tissue infections and mixed staphylococcal/Gram-negative infections and aerobic/anaerobic infections.
Ticarcillin-clavulanate and Piperacillin-tazobactam	High	P1, T2, R2	Valuable agents for a range of severe mixed aerobic-anaerobic infections including intra-abdominal infections, aspiration pneumonia, skin/soft tissue infections. Neutropenic sepsis.
1st Generation Cephalosporins			
Cephalexin, cephalothin and cephazolin	Medium	P3, T3, R1	Treatment of minor and staphylococcal infections in penicillin-allergic patients. Prophylaxis in orthopaedic and other surgery
2nd Generation Cephalosporins			
Cephamandole, cefaclor and cefuroxime-axetil	Medium	P0, T2, R1	Treatment of respiratory infections in penicillin-allergic patients
Cephamycins			
Cefoxitin and cefotetan	Medium	P3, T1, R2	Useful anti-anaerobic activity, major role in surgical prophylaxis
3rd Generation Cephalosporins			
Ceftriaxone	High	P2, T3, R2	Major agent in severe pneumonia and meningitis. Used in selected cases for treatment of gonorrhoea and alternative for prophylaxis of meningococcal infection
Cefotaxime	High	P0, T3, R2	Major agent in severe pneumonia and meningitis
4th Generation Cephalosporins (anti pseudomonal)			
Ceftazidime, cefpirome and cefepime	High	P1, T3, R3	Restricted role in pseudomonal infection and neutropenic sepsis
Carbapenems			
Imipenem, meropenem and ertapenem	High	P0, T3, R4	Very broad-spectrum reserve agents for serious Gram-negative infections
Monobactams			
Aztreonam	High	P0, T3, R4	Reserve agents for resistant Gram-negative infections or patients with severe ß-lactam allergy
Tetracyclines			
Doxycycline, minocycline, and tetracycline (demeclocycline)	Low	P2, T3, R1	Major agents for minor respiratory tract infections and acne. Supportive role in pneumonia for treating *Mycoplasma* and *Chlamydia pneumoniae.* Malaria prophylaxis (doxycycline)
Glycopeptides			
Vancomycin	High	P2, T3, R2	Drug of choice for serious methicillin-resistant staphylococcal infections. Reserve agent for enterococcal infection when there is

Antibiotic	EAGAR Rating	Uses P, T, R	Comments on Use in Human Medicine
			resistance or penicillin allergy
Teicoplanin	High	P1, T1, R4	Substitute for vancomycin if intolerance or outpatient IV therapy
Aminoglycosides			
Neomycin (including framycetin)	Low	P1, T2, R1	Topical agent for skin infection and gut suppression
Gentamicin and tobramycin	Medium	P2, T3, R1	Standard agents in combination for serious and pseudomonal infection. Gentamicin used in combination for endocarditis
Netilmicin, amikacin	High	P0, T2, R4	Reserve agents for Gram-negatives resistant to gentamicin and tobramycin
Spectinomycin	Medium	P0, T2, R1	Spectinomycin only used for gonorrhoea (infrequently)
Streptomycin	Low	P0, T1, R4	Rare use in treatment of TB and enterococcal endocarditis
Capeomycin	Low	P0, T1, R4	Rare use in TB
Paromomycin	Low	P0, T1, R4	Rare use for *Cryptosporidium* infection
Sulfonamides and DHFR inhibitors			
Sulfadiazine	Low	P0, T3, R4	Treatment of acute toxoplasmosis
Trimethoprim	Low	P2, T3, R1	Treatment and prophylaxis of UTI
Trimethoprim-sulfamethoxazole (co-trimoxazole)	Low	P2, T3, R1	Minor infections, especially treatment and prophylaxis of UTI. Standard for treatment and prophylaxis of *Pneumocystis carinii* infection and nocardiasis
Sulfadoxine-pyrimethamine	Low	P3, T2, R3	Treatment and prophylaxis of malaria
Proguanil	Low	P3, T1, R4	Malaria prophylaxis
Oxazolidinones			.
Linezolid	High	P0, T1, R4	Treatment of multi-resistant Gram-positive infections, especially MRSA and VRE
Macrolides			
Azithromycin	Low	P2, T2, R2	Treatment of *Chlamydia trachomatis* infections. Major agent for treatment and suppression of atypical mycobacterial infection
Clarithromycin	Low	P2, T2, R1	Treatment of minor Gram-positive infections. Major agent for treatment and suppression of atypical mycobacterial infection
Erythromycin and roxithromycin	Low	P1, T3, R1	Treatment of minor Gram-positive, *Chlamydia* and *Mycoplasma* infections.
Lincosamides			
Clindamycin and lincomycin	Medium	P1, T3, R2	Reserved for Gram-positive and anaerobic infections in penicillin-allergic patients. Clindamycin topical used for acne
Nitroimidazoles			
Metronidazole and tinidazole	Medium	P2, T3, R1	Major agents for the treatment and prevention of anaerobic infections in hospitals. Principal agents for the treatment of giardiasis and trichomoniasis
Quinolones			
Nalidixic acid	Medium	P1, T2, R1	Use confined to treatment and prophylaxis of UTI
Fluoroquinolones			
Norfloxacin	High	P1, T3, R2	Treatment and prevention of complicated UTI
Ciprofloxacin	High	P2, T3, R3	Major oral agent for the treatment of Gram-negative infections resistant to other agents. Minor role in meningococcal prophylaxis
Gatifloxacin and moxifloxacin	High	P0, T3, R4	Restricted role in the management of serious respiratory infections, especially pneumonia in patients with severe penicillin allergy
Ofloxacin	High	P0, T2, R3	Topical treatment of severe eye infections
Streptogramins			
Quinupristin with dalfopristin	High	P0, T1, R4	Reserve agent for multi-resistant Gram-positive infections (MRSA and vancomycin-resistant *Enterococcus faecium*)
Antimycobacterials			
Isoniazid	High	P2, T3, R4	Primary agent for treatment and prevention
Ethambutol and pyrazinamide	High	P1, T3, R4	Primary agent for treatment of TB

Antibiotic	EAGAR Rating	Uses P, T, R	Comments on Use in Human Medicine
Cycloserine, p-aminosalicylic acid, and prothionamide	High	P0, T1, R4	Reserve agents for complicated or resistant TB
Antileprotics			
Clofazimine and dapsone	High	P0, T3, R4	Usage predominantly for treatment of leprosy
Ansamycins (Rifamycins)			
Rifampicin (Rifampin)	High	P3, T3, R2	Meningococcal and *H. influenzae* type b prophylaxis; Standard part of TB regimens; Important oral agent in combination for MRSA infections
Rifabutin	High	P3, T2, R4	Treatment and prophylaxis of *Mycobacterium avium* complex infections
Polypeptides			
Bacitracin, gramicidin,	Low	P0, T2, R1	Topical agents with Gram-positive activity
Polymyxin B	Low	P0, T2, R1	Topical agent with Gram-negative activity
Colistin	High	P0, T1, R2	Reserve agent for multi-resistant *Pseudomonas aeruginosa* infection (both inhaled and intravenous)
Amphenicols			
Chloramphenicol	Low	P0, T2, R1	Usage largely as topical eye preparation. Occasional need for the treatment of bacterial meningitis
Nitrofurans			
Nitrofurantoin	Low	P2, T2, R1	Treatment and prophylaxis of urinary tract infections only
Fusidanes			
Sodium fusidate	High	P0, T3, R2	Used in combination therapy with rifampicin for MRSA

Abbreviations: UTI = urinary tract infections, TB = tuberculosis, MRSA = methicillin-resistant *Staphylococcus aureus*, VRE = vancomycin resistant *Enterococcus* species

LEGEND for TABLE

EAGAR Importance Rating

High

These are essential antibiotics for treatment of human infections where there are few or no alternatives for many infections. Also have been called "critical", "last-resort" or "last line" antibiotics.

Medium

There are other alternatives available but less than for those classified as Low;

Low

There are a reasonable number of alternative agents in different classes are available to treat most infections even if antibiotic resistance develops

Human Uses

These reflect the current use of these antibiotics in Australia in human medicine. It does not necessarily reflect what EAGAR believes should be the uses of these agents or what restrictions should apply to their use.

P: prophylactic use

0 = not recommended for prophylactic use
1 = rarely used
2 = moderate
3 = frequent or major use

T: therapeutic use

1 = infrequently used for listed indications
2 = moderate use for listed indications
3 = used frequently for listed indications

R = Restriction on use (Pharmaceutical Benefits Scheme or hospitals)

1 = readily available
2 = some extra rules on use e.g. 'Restricted benefit' in the Pharmaceutical Benefits Scheme (PBS) or not listed on the PBS and therefore not subsidised
3 = higher level of restriction e.g. needs an 'Authority required' prescription on the PBS or not listed on the PBS and therefore not subsidised; often restricted use in hospitals
4 = use severely restricted (e.g. not available for prescription under PBS, available in major hospitals but only with permission from microbiologist or infectious diseases consultant, or in a special clinic).

Reference

Therapeutic Guidelines – Antibiotic. Version 12, 2003. Therapeutic Guidelines Limited, Melbourne (www.tg.com.au)